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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/622,373	07/18/2003	Jennifer L. Whistler	12101-011-999	4987

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EXAMINER	
ULM, JOHN D	
ART UNIT	PAPER NUMBER
1649	
MAIL DATE	DELIVERY MODE
05/22/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/622,373	WHISTLER ET AL.	
	Examiner	Art Unit	
	John D. Ulm	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3/28/08*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,10,11,13-18,24,25 and 27-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,10,11,13-18,24,25 and 27-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/2808*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1) Claims 1, 10, 11, 13 to 18, 24, 25 and 27 to 29 are pending in the instant application. Claims 1, 10, 11, 16 and 18 have been amended and claims 2 to 9, 12, 19 to 23 and 26 have been canceled and as requested by Applicant in the correspondence filed 28 March of 2008.

2) Any objection or rejection of record that is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

3) The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Continued Examination Under 37 CFR 1.114

4) A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 28 March of 2008 has been entered.

Claim Rejections - 35 USC § 112

5) Claims 1, 10, 11 and 13 to 17are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. These claims encompass subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. These claims are not enabled because

they expressly require a "polypeptide comprising the amino acid sequence of SEQ ID NO: 8" and there is no amino acid sequence presented in SEQ ID NO:8 of the instant application. The sequence presented in SEQ ID NO:8 of the instant application is a nucleotide sequence. Clearly, an artisan can not produce a polypeptide comprising an amino acid sequence that does not exist.

Claims 18, 24, 25 and 27 to 29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In so far as claims 18, 24 and 27 to 29 encompass a "method of enhancing agonist-induced down-regulation of a G protein-coupled receptor" by exogenously administering a "GASP1" polypeptide comprising the amino acid sequence of SEQ ID NO:2 thereto either *in vivo* or *in vitro*, the instant specification is not enabling for those reasons of record. As stated previously, the site of interaction between a GASP protein of the instant invention and a delta opioid receptor is intracellular. The only compounds that are described in the instant specification that have the activities required by the instant claims are polypeptides. One of ordinary skill in the art of molecular biology has no reasonable expectation that an exogenously administered polypeptide of the instant invention will have any effect whatever on the intracellular interaction of a delta opioid receptor with any GASP protein contained within that cell, as would be required for the functionality of the claimed method. The instant specification nether discloses how to

obtain the cellular internalization of a polypeptide of the instant invention nor identifies any prior art reference in which an analogous method has been practiced with a different peptide. The amino acid sequence presented in SEQ ID NO:2 is over **fourteen hundred amino acids in length**. Because neither the specification nor the art of record describes even a single instant in which a protein of such magnitude has been successfully introduced into a cell by the exogenous administration of that protein, and because the instant specification fails to provide any sound scientific rationale that would support a conclusion that a protein of such size would be taken up by a cell to which it has been administered, one of ordinary skill has absolutely no expectation of achieving the result recited in these claims via the exogenous administration of a GASP1 polypeptide comprising SEQ ID NO:2.

Applicant urges that the "specification discloses data to show that GASP 1 polypeptides can modulate agonist-induced down regulation of PCR by regulating endocytosis of GPCRs in cell lines overexpressing GASP 1 polypeptides". Applicant relies upon the He et al. publication (Cell 108(2):271-282, 2002) to show that "it was known in the art that peptides that are capable of regulating endocytosis of GPCRs *in vitro*, such as enkephalin, can also regulate endocyotosis of GPCRs *in vivo*". These arguments are not persuasive because the site of action of enkephalin, a synthetic peptide of only three amino acids in length, is on the outside of the cell surface and, therefore, available to interact with exogenously applied enkephalin. This is not the case with the GAST1 polypeptide of the instant invention, as explained above.

Applicant has traversed this rejection on the premise that "based on the teachings in the specification, it is clear that a sufficient guidance is provided in the specification so as to allow those of ordinary skill in the art to make and use the claimed invention". Such an argument is not persuasive because it fails to address the technical merits of the rejection. Applicant's reliance on *In re Brana*, 51 F.3d 1560,1566, 34 USPQ2d 1436 ,1441 (Fed. Cir. 1995) is misplaced. That court decision determined that a compound which belonged to a family of compounds known to have anti-tumor activity, which is a common and well established specific and substantial utility for that family of compounds, would be reasonably expected to have anti-tumor activity in light of positive *in vitro* data with respect to that particular compound since that data has proven to be an indicator of anti-cancer activity by other members of that family. Since Applicant has failed to show that the exogenous administration of a GASP1 polypeptide comprising SEQ ID NO:2 of the instant application to a cell *in vitro* has the required effect upon that cell, Applicant can not rely upon those results to argue that they are predictive of *in vivo* activity.

In so far as claims 18, 25 and 27 to 29 encompass a "method of enhancing agonist-induced down-regulation of a G protein-coupled receptor" by exogenous administration of a polynucleotide encoding a GASP1 polypeptide comprising SEQ ID NO:2 to a cell *in vivo*, they are not enabled for those reasons of record. As stated previously, one of ordinary skill would not reasonably expect the exogenous administration of a nucleic acid encoding all or part of a polypeptide of the instant invention to a mammal to have a clinical effect because the art of gene therapy has not

developed to the level of a routine practice in the clinical arts. It is noted that several genetic defects associated with diseases such as sickle cell anemia and cystic fibrosis are well known in the art, as are the genetic corrections needed to cure these diseases, and yet the art of record does not show that these diseases have been successfully treated by gene therapy. It is further noted that a number of proteins that are critical to the proliferative and invasive nature of cancer cells, such a telomerases and angiogenesis stimulators, have been well characterized in the art of molecular biology before the making of the instant invention and yet the art of record does not describe a single instance in which a cancer has been successfully treated by genetic therapy. As stated above, the claimed method is not enabled because one of ordinary skill in the art of molecular biology can not follow the guidance provided by the instant specification, combined with a routine knowledge of the art, and practice in claimed method with any reasonable expectation of success.

As state in the previous office action, A patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the decision of *Genentec, Inc, v. Novo Nordisk*, 42 USPQ 2d 100,(CAFC 1997), the court held that:

> "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure". The court further stated that "when there is no disclosure of any specific starting material or of any of the conditions under which a process is to be carried out, undue experimentation is required; there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the

disclosure related to the process is within the skill of the art", "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

The instant specification is not enabling because one can not following the guidance presented therein and practice the claimed method without first making a substantial inventive contribution.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6) Claims 1, 10, 11 and 13 to 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims are vague and indefinite because there is no antecedent basis for "the amino acid sequence of SEQ ID NO:8", which is a nucleotide sequence.

Response to Arguments

7) Applicant's arguments filed 28 March of 2008 have been fully considered but they are not persuasive.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John D. Ulm whose telephone number is (571) 272-0880. The examiner can normally be reached on 9:00AM to 5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/John D. Ulm/

Primary Examiner, Art Unit 1649